

## One-Carbon Ring Expansion in Cyclopentanones as a Free-Radical Clock

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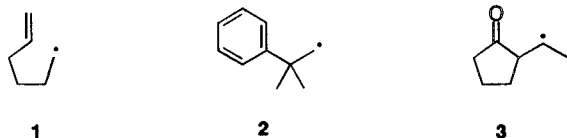
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### Introduction

Free radicals are of considerable importance in the development of organic chemistry, and many radical-based strategies employ group-14 hydrides.<sup>2</sup> One of the propagation steps of these radical chain reactions is the hydrogen transfer from the reducing agent to a radical (eq 1). To modulate the hydrogen donating abilities of the hydrides, a significant number of substrates has been introduced.<sup>3,4</sup>



An indirect procedure for measuring the rate constant of eq 1 involves a competition between this process and a unimolecular path of the radical (free-radical clocks).<sup>5</sup> In his review Newcomb summarized competition methods as well as calibrated unimolecular rearrangements of radicals for this purpose.<sup>3</sup> Kinetic scales for alkyl radical reactions span literally the entire range of radical kinetics in solution. The most popular example of primary alkyl radicals is the 5-exo cyclization of the 5-hexenyl radical (**1**) for which the rate constant of  $2.3 \times 10^5 \text{ s}^{-1}$  at 298 K<sup>6</sup>



is useful for middle regions of the kinetic scale. In a few cases, the presence of an external double bond has caused some inconvenience due to the similar reactivities of bromine abstraction from 5-hexenyl bromide and addition to the double bond.<sup>7</sup> In principle, this inconvenience can be overcome by using the neophyl radical (**2**) rearrangement.<sup>8</sup> However, this process occurs with a rate constant of  $9.0 \times 10^2 \text{ s}^{-1}$  at 298 K, which is generally useful for

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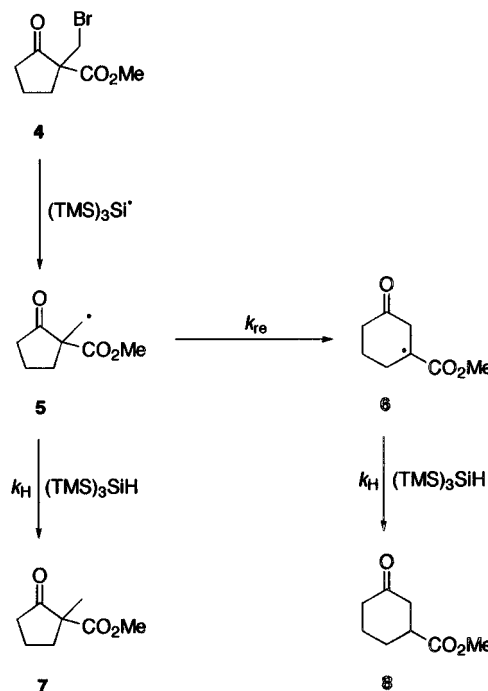
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### Scheme 1



**Table 1. Kinetic Data for the Reaction of Bromide 4 with  $(\text{TMS})_3\text{SiH}$  in Toluene or Benzene at Various Temperatures<sup>a</sup>**

T, K	$k_{\text{H}}/k_{\text{re}},^b \text{ M}^{-1}$	T, K	$k_{\text{H}}/k_{\text{re}},^b \text{ M}^{-1}$
333	4.11	383	1.96
343	3.19	393	2.11
353	2.75	403	1.43
363	2.77	413	1.37

<sup>a</sup> Range of silane concentration, 0.5–0.9 M. <sup>b</sup> Average of several different experiments (at least four).

low regions of the kinetic scale. Therefore, it was necessary to identify a free-radical clock (i) that does not involve carbon–carbon double bonds, (ii) for which the unimolecular rearrangement is ca.  $10^5 \text{ s}^{-1}$  at room temperature, and (iii) for which the starting bromide is easily accessible.

A general method of one-carbon ring expansion of cycloketones was introduced in 1987 concurrently by Beckwith<sup>9</sup> and Dowd<sup>10</sup> and later showed to be a powerful synthetic tool.<sup>11</sup> We have recently studied these reactions from the mechanistic point of view, showing that the ring expansion occurs via three-membered cyclic intermediate radicals (or transition states), excluding the intermediacy of acyl radicals.<sup>12</sup> Furthermore, by using free-radical clock methodology we have obtained the Arrhenius parameters for the ring expansion of the secondary alkyl

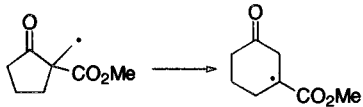
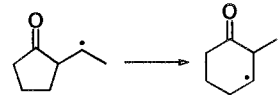
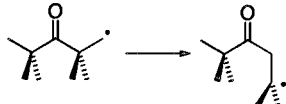
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**Table 2.** Arrhenius Parameters for One-Carbon Ring Expansion and Related Systems<sup>a</sup>

Reaction	log (A/s <sup>-1</sup> )	E, kcal/mol	k <sup>298K</sup> , s <sup>-1</sup>	Ref.
	10.56 ± 0.57	7.97 ± 0.88	5.2 × 10 <sup>4</sup>	this work
	10.51 ± 0.45	9.39 ± 0.59	4.2 × 10 <sup>3</sup>	12
	10.94 ± 0.49	7.77 ± 0.75	1.7 × 10 <sup>5</sup>	16

<sup>a</sup> Errors correspond to one standard deviation.

radical **3**. The rate constant is  $4.2 \times 10^3 \text{ s}^{-1}$  at 298 K. We envisaged that the analogous primary alkyl radical should have a rate constant of the ring expansion in the desired kinetic range of a free-radical clock ( $10^4$ – $10^5 \text{ s}^{-1}$ ). Therefore, we chose to test the Dowd rearrangement **5** → **6** (Scheme 1), since the access to the starting bromide **4** is straightforward from  $\beta$ -keto ester by Dieckmann condensation.<sup>10</sup>

In this paper competitive kinetic studies on the calibration of one-carbon ring expansion of reaction **5** → **6** are reported, and by using these data, the measurements of rate constants for the hydrogen abstraction from some silanes and phosphites, which were not yet available, were carried out.

## Results and Discussion

**Kinetics for the Ring Expansion.** A rate constant for the ring expansion can be obtained, providing that conditions can be found in which the intermediate radical **5** is partitioned between the two reaction channels (Scheme 1), that is, reaction with the silicon hydride and ring expansion. To determine the kinetics of the rearrangement of **5** into **6** under pseudo-first-order conditions, a series of experiments was conducted in which the bromide **4** was treated with a large excess of tris(trimethylsilyl)silane in known concentrations at various temperatures, i.e.,  $[(\text{TMS})_3\text{SiH}]_0 \geq 20 \times [\mathbf{4}]_0$ . Compounds **7** and **8** were the reduction products, the relative concentrations of which varied in the expected manner at each temperature as the concentration of  $(\text{TMS})_3\text{SiH}$  changed from 0.5 to 0.9 M. Since the silane concentration remained essentially constant under our experimental conditions, the following relation is obeyed:<sup>3</sup>

$$[\mathbf{7}]_f/[\mathbf{8}]_f = k_{\text{H}}/k_{\text{re}}[(\text{TMS})_3\text{SiH}]_0 \quad (2)$$

where  $[\mathbf{7}]_f$  and  $[\mathbf{8}]_f$  represent the final concentrations of the two products. The  $k_{\text{H}}/k_{\text{re}}$  ratios reported in Table 1 were obtained as the average of several different experiments (at least four). Linear regression analysis of a

$\log(k_{\text{H}}/k_{\text{re}})$  vs  $1/T$  plot yields the relative Arrhenius parameters given by eq 3, where  $\theta = 2.3RT \text{ kcal mol}^{-1}$  and the errors correspond to one standard deviation.

$$\log k_{\text{H}}/k_{\text{re}} (\text{M}^{-1}) = - (1.70 \pm 0.21) + (3.50 \pm 0.35)/\theta \quad (3)$$

Combination of the Arrhenius expression for  $k_{\text{H}}/k_{\text{re}}$  with the known Arrhenius parameters for the reaction primary alkyl radical<sup>13</sup> with  $(\text{TMS})_3\text{SiH}$ <sup>14</sup> yields the temperature dependence of  $k_{\text{re}}$  (Table 2). The value of  $k_{\text{re}}$  can be calculated as  $5.2 \times 10^4 \text{ s}^{-1}$  at 298 K.

The Arrhenius parameters obtained for the ring expansion **5** → **6** can be compared with those reported for the ring expansion of secondary alkyl radicals and for 1,2-acyl migration in the acyclic system (Table 2). The three  $A$  factors are within the experimental error and in the expected range for a three-membered transition state. However, the small difference may be significant, since in the transition state of the acyclic rearrangement two C–C bond rotations must be “frozen”, whereas in the transition states of ring expansions one C–C bond rotation plus the entire ring must be “frozen”. The higher barrier (ca. 1.5 kcal/mol) for the ring expansion of the secondary alkyl radical compared to the ring expansion of the primary alkyl radical and to 1,2-acyl migration should reflect the nature of the attacking alkyl radical, although the “*gem*-dimethyl accelerating factor” in the last two cases might play a role.<sup>17</sup>

### Kinetics for Some Hydrogen Atom Abstractions.

To determine the kinetics of hydrogen abstraction from some hydrides by radical **5**, a series of similar experiments was conducted in which the bromide **4** was treated

(14) The temperature-dependent function for the reaction of 5-hexenyl radicals with  $(\text{TMS})_3\text{SiH}$  is as follows:  $\log k_{\text{H}} (\text{M}^{-1} \text{ s}^{-1}) = (8.86 \pm 0.36) - (4.47 \pm 0.53)/\theta$ , where  $\theta = 2.3RT \text{ kcal/mol}$ .<sup>15</sup> Errors correspond to one standard deviation.

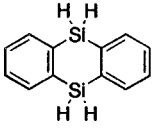
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(13) On the basis of the assumption that the radical **5** will react with  $(\text{TMS})_3\text{SiH}$  at the same rate as that measured from 5-hexenyl radical.

**Table III. Kinetic Data for Some Hydrogen Atom Abstractions by Radical 5 in Benzene**

XH	T, K	[XH], <sup>a</sup> M	$k_H/k_{re}$ , <sup>b</sup> M <sup>-1</sup>	$k_H$ , M <sup>-1</sup> s <sup>-1</sup>
(MeS) <sub>3</sub> SiH	353	0.08 - 1.88	0.93	$3.9 \times 10^5$
( <i>n</i> -PrS) <sub>3</sub> SiH	353	0.62 - 1.24	0.88	$3.7 \times 10^5$
	353	0.05 - 0.38	5.03	$2.1 \times 10^6$
(MeO) <sub>2</sub> P(O)H	403	4.14 - 8.29	0.07 <sup>c</sup>	$1.2 \times 10^5$
(EtO) <sub>2</sub> P(O)H	403	2.80 - 5.43	0.07	$1.2 \times 10^5$

<sup>a</sup> Range of concentrations employed. <sup>b</sup> Average of several different experiments (at least four). <sup>c</sup> In chlorobenzene.

with a large excess of some silanes and phosphites in known concentrations at 353 and 403 K, respectively. The  $k_H/k_{re}$  ratios are summarized in Table 3. Taking  $k_{re}$  for reaction **5** → **6** from Table 2,  $k_H$  values were calculated and are reported in Table 3.

Tris(alkylthio)silanes were found to be effective radical-based reducing agents for a variety of organic substrates.<sup>7a</sup> From Table 3 it can be seen that their hydrogen-donor abilities are independent of the nature of the alkyl groups attached to the sulfur atoms and are comparable to that of (TMS)<sub>2</sub>Si(H)Me.<sup>18</sup> 5,10-Dihydrosilanthrene was found to effectively replace Bu<sub>3</sub>SnH in the deoxygenation of secondary alcohols via thiono esters (Barton–McCombie reaction), and the rate constant of its reaction with the secondary alkyl radical **3** was found to be  $2.6 \times 10^5$  M<sup>-1</sup>

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s<sup>-1</sup> at 373 K.<sup>19</sup> Therefore, the primary alkyl radical **5** reacts ca. 8 times faster than the secondary alkyl radical **3** at ca. 353 K with 5,10-dihydrosilanthrene, and its hydrogen-donor ability is comparable to that of (TMS)<sub>3</sub>SiH.<sup>18</sup> It is worth pointing out that 5,10-dihydrosilanthrene is more than 1 order of magnitude more reactive than Ph<sub>2</sub>SiH<sub>2</sub> toward alkyl radicals (taking into account the statistical number of hydrogen abstractions). The reason for this enhancement in the reactivity is probably due to the stabilization of silyl radical induced by a transannular interaction of the vicinal Si substituent.<sup>18</sup>

Barton et al. have recently used dialkyl phosphites as reducing agents for radical deoxygenations, dehalogenations, and deaminations.<sup>20</sup> Phosphinoyl radicals are much less reactive than group-14 centered radicals toward halides (3–4 orders of magnitude with respect to silyl radicals).<sup>21</sup> On the other hand, the rate constants for addition to double bonds are comparable.<sup>21</sup> The rate constants for the reaction of radical **5** with dialkyl phosphites were found to be ca.  $1 \times 10^5$  M<sup>-1</sup> s<sup>-1</sup> at 403 K and their hydrogen-donor abilities are comparable to phenyl-substituted silanes.<sup>18</sup>

### Experimental Section

**Kinetic Experiments.** Toluene or benzene containing a small amount of nonane, decane, or undecane as an internal GC standard was used as solvent. The hydrogen donor and compound **4** were added in a ratio of ≥20:1. Samples of these reaction mixtures were degassed in Wheaton reactors. Reactions were initiated thermally (AIBN or di-*tert*-butyl peroxide). The products of interest were identified by comparison of their retention times with authentic materials.

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